Interactions of Poly(amidoamine) Dendrimers with Human Serum Albumin: Binding Constants and Mechanisms

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Supporting Information

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Table S1. Partial solvent accessible areas (PSASA) relative to H2 (defined as 100) calculated using atomistic molecular dynamics (MD) simulations. Various probe radii (p= 1.4- 48 Å) were used in PSASA analysis. For comparison, the relative strength of interactions between G4-NH_2 PAMAM and HSA calculated from the epitope mapping in the NMR experiment is shown. The best agreement between the MD and the NMR results is achieved when p= 12 Å is used, which corresponds to the van der Waals radius of a HSA molecule.

H type	NMR	MD					
		1.4	3	6	12	24	48
H1	**82.4**	82.4	75.3	61.1	**58.4**	83.2	65.7
H2	**100.0**	100.0	100.0	100.0	**100.0**	100.0	100.0
H3	**92.3**	101.2	91.6	77.9	**94.3**	143.5	117.3
H4	**74.4**	102.8	95.2	89.8	**77.3**	154.7	122.9

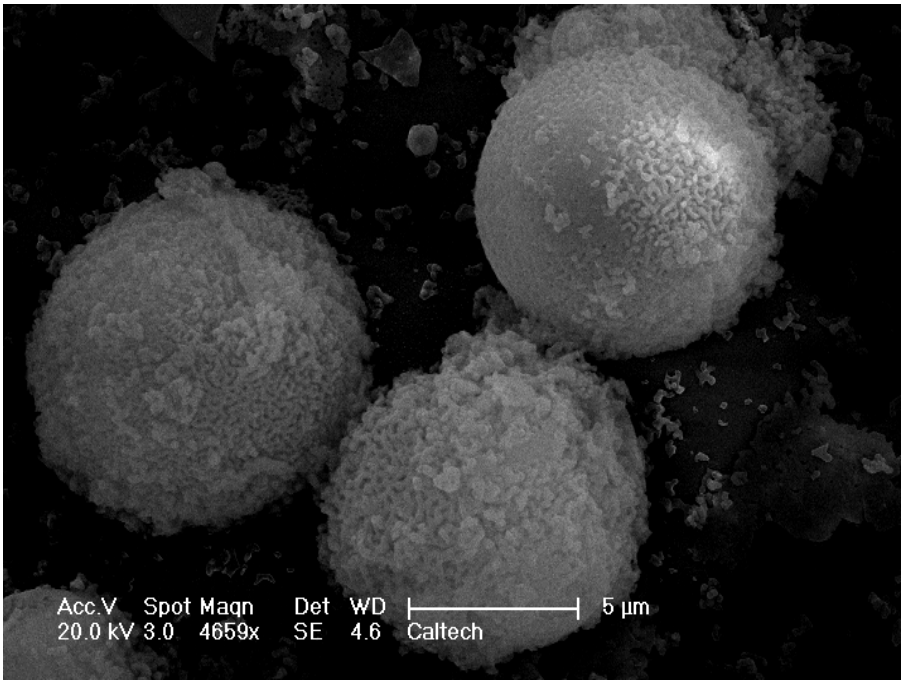

Figure S1. Typical SEM image of an HSA coated silica beads (Transil albumin kit).

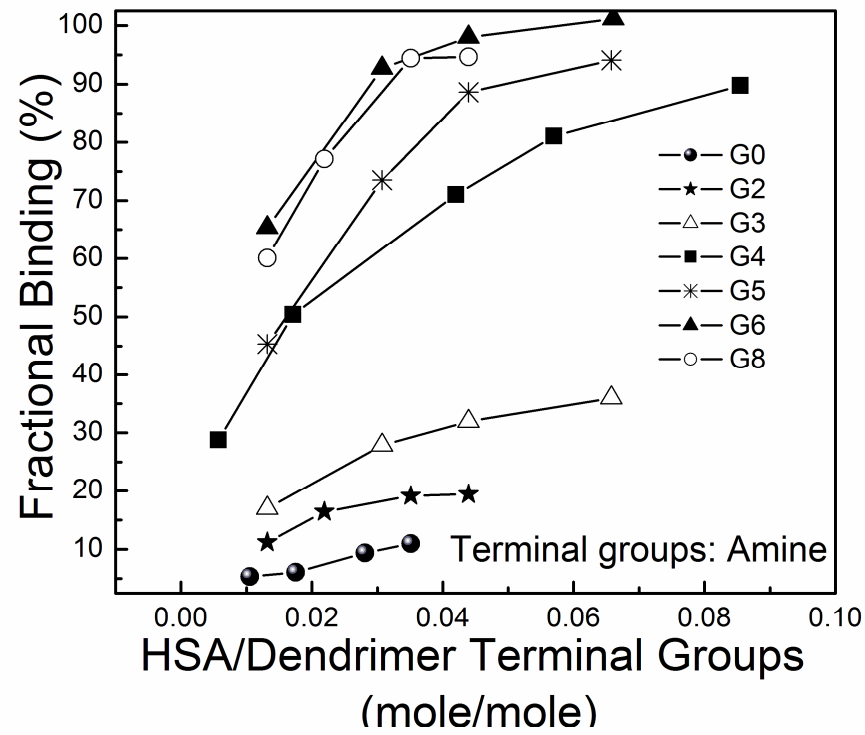

Figure S2. Fractional binding (FB) of Gx-NH_2 PAMAM dendrimers to HSA as a function of generation and protein-dendrimer molar ratio. In all experiments, the concentration of dendrimer terminal amine groups (NH_2) was kept constant at 64 μM.

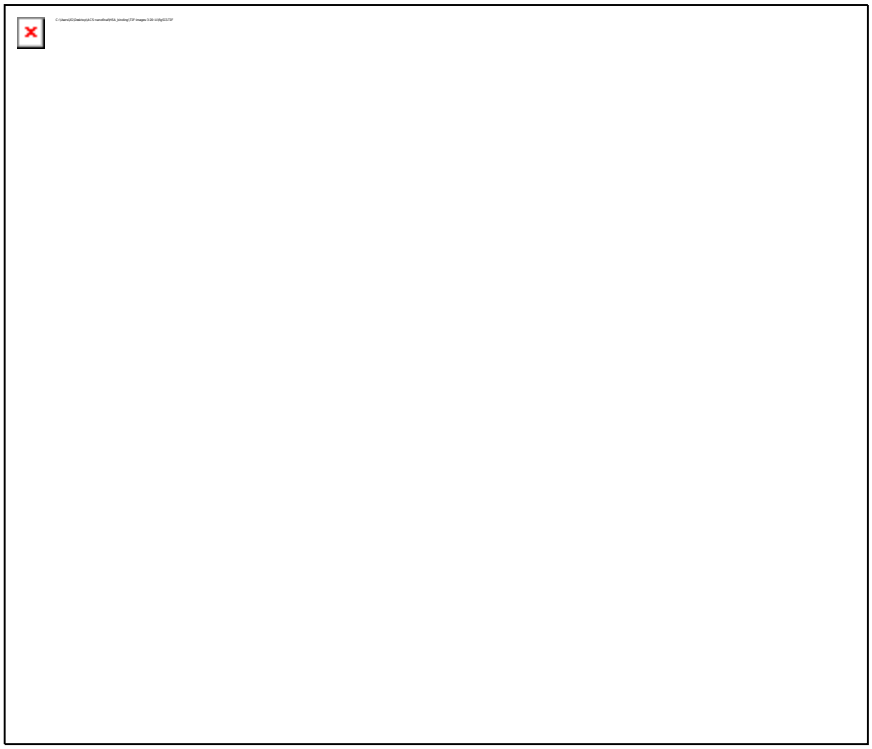

Figure S3. Fractional binding (FB) of G4-X and G3.5 PAMAM dendrimers to HSA as a function terminal group chemistry and protein-dendrimer molar ratio. In all experiments, the concentration of dendrimer terminal amine groups (X and COONa) was kept constant at 64 μM.

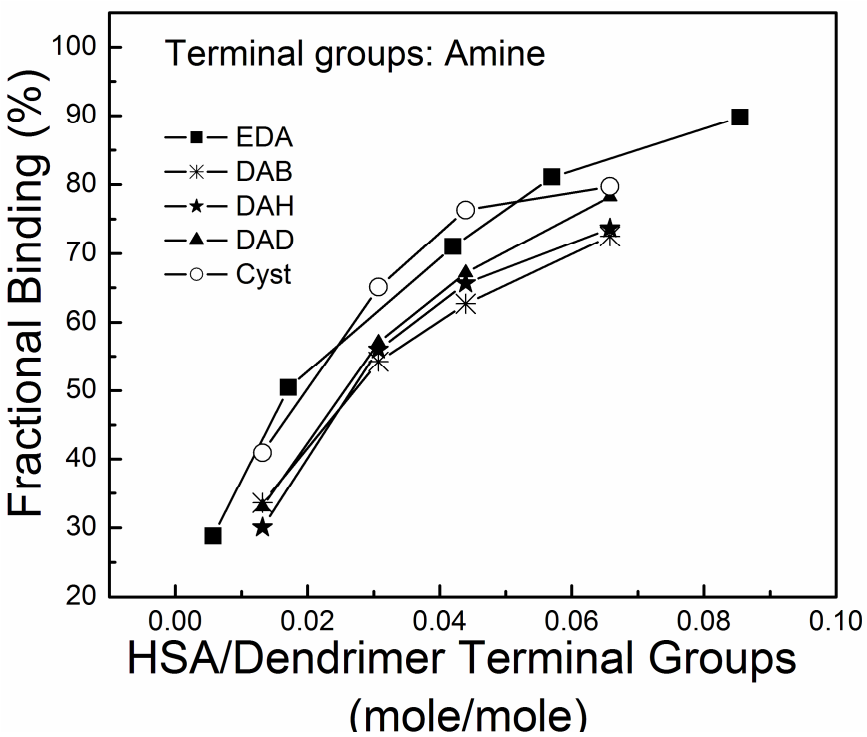

Figure S4. Fractional binding (FB) of G4-NH_2 PAMAM dendrimers to HSA as a function of core chemistry and protein-dendrimer molar ratio. In all experiments, the concentration of dendrimer terminal amine groups was kept constant at 64 μM.

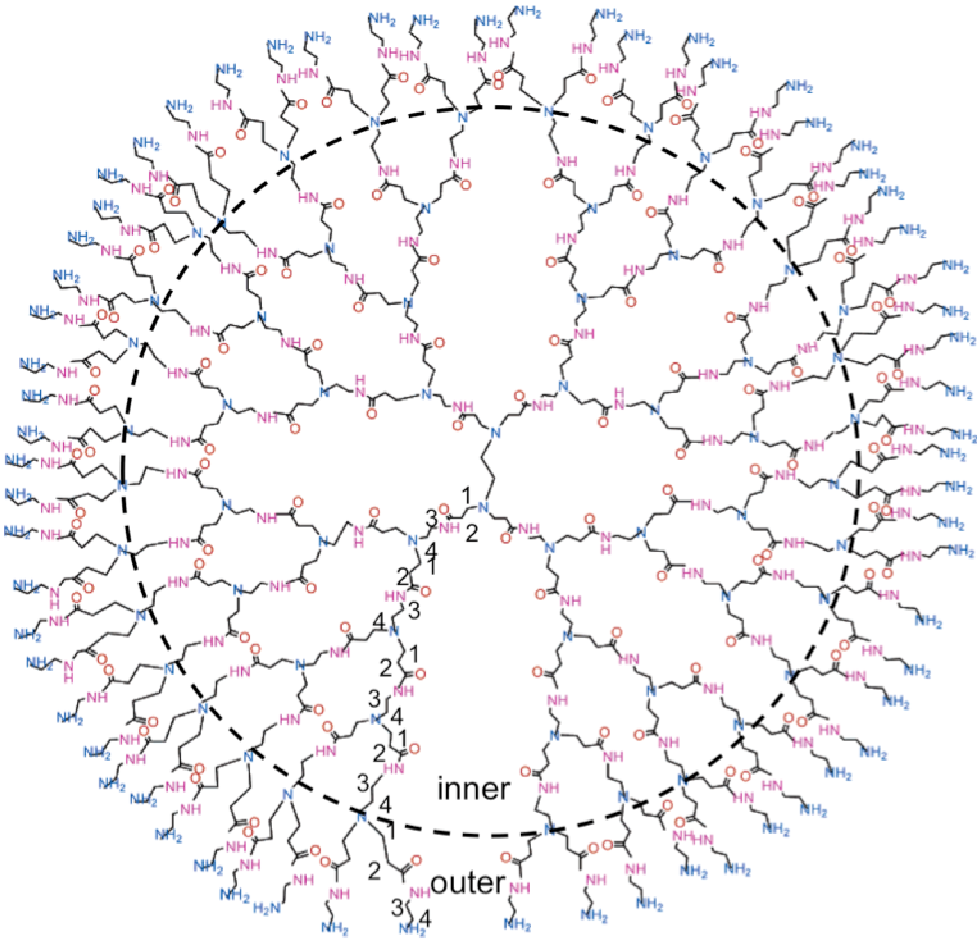

Figure S5. 2-D structure of a G4-NH_2 PAMAM dendrimer with CH_2 groups labeled as 1, 2, 3 and 4. The terminal groups of the dendrimer outside the dash circle are denoted as outer shells, while the others within the dash circle are denoted as inner shells.

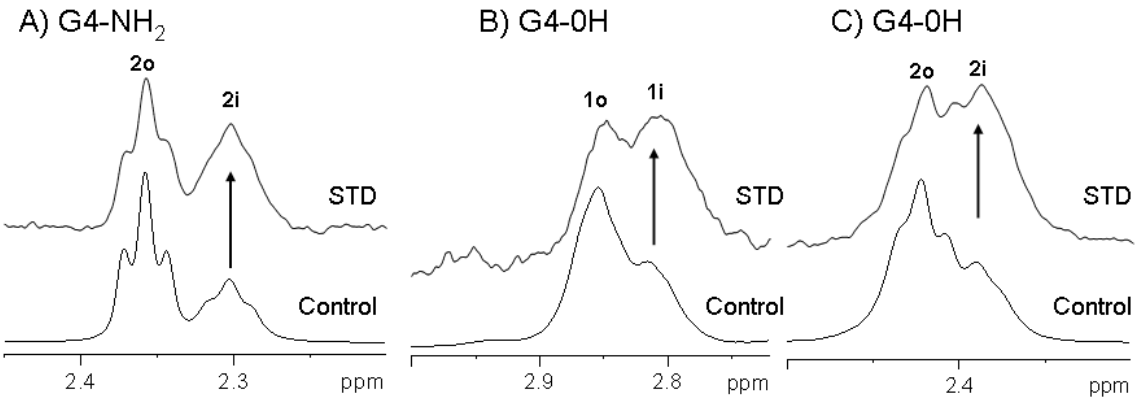

Figure S6. Comparison of control and STD NMR spectra for protons β and γ from the amide groups. Protons 17 and 18 have been labeled as examples for one of the branches (see Figure 7 for numbering scheme). The symbols o and i indicate, respectively, protons in the dendrimer outermost shell and all other inner shells (See Figure S5). In the STD NMR spectrum only signal from interacting protons are observed. The inner protons are clearly enhanced in the STD spectra indicating they have a higher affinity for the HSA than protons in the outer shell of the dendrimer.

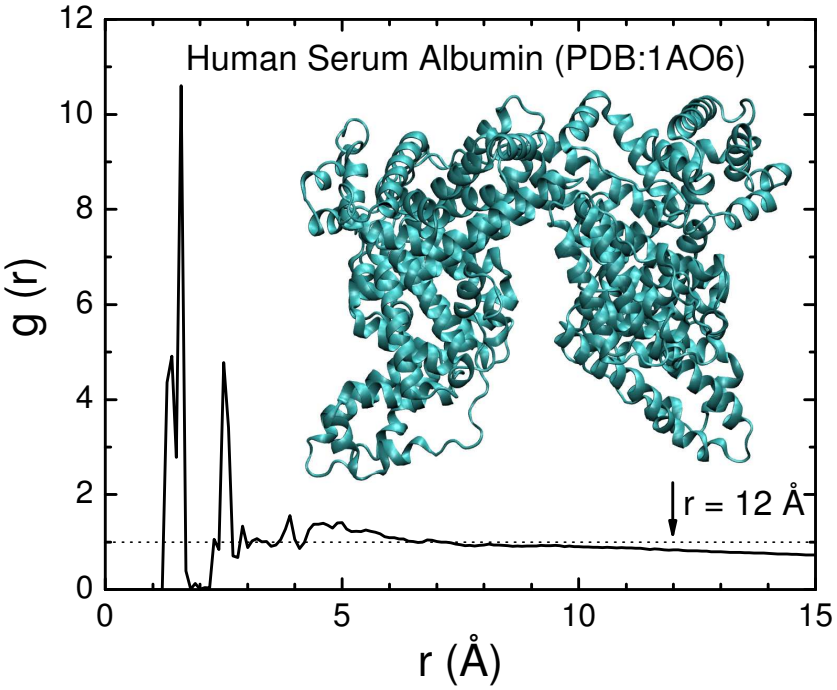

Figure S7. Radial distribution function of a human serum albumin (HSA) molecule (PDB code: 1AO6). The structure of HSA molecule is shown in the insert. The vdW radius of HSA is estimated to be 12 Å.

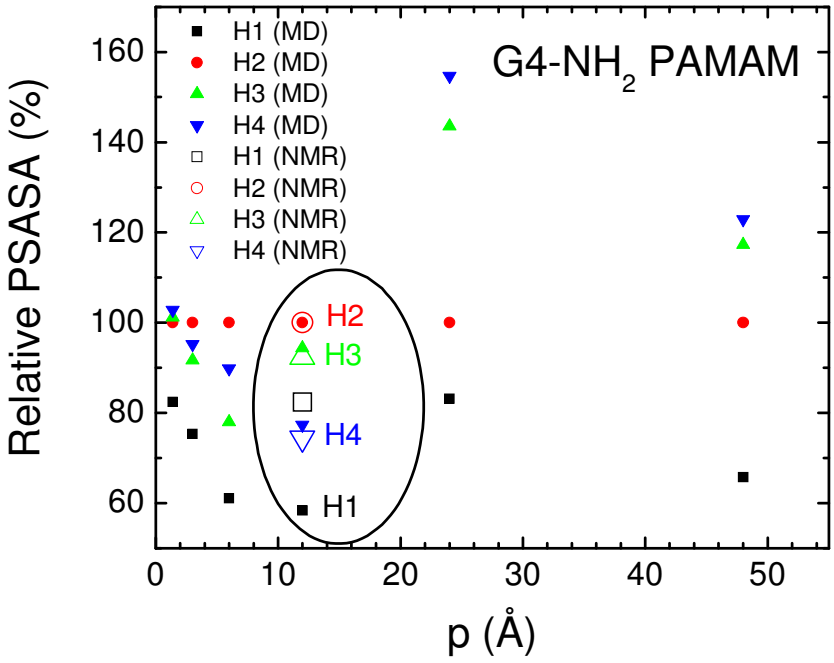

Figure S8. Partial solvent accessible surface area (PSASA) of the protons of CH_2 groups of G4-NH2 PAMAM dendrimer relative to H2 (defined as 100). The hydrogen atom type goes outward topologically in the order of H1, H2, H3, and H4. The best agreement between the MD and the NMR results is achieved when p= 12 Å as shown within the circle.

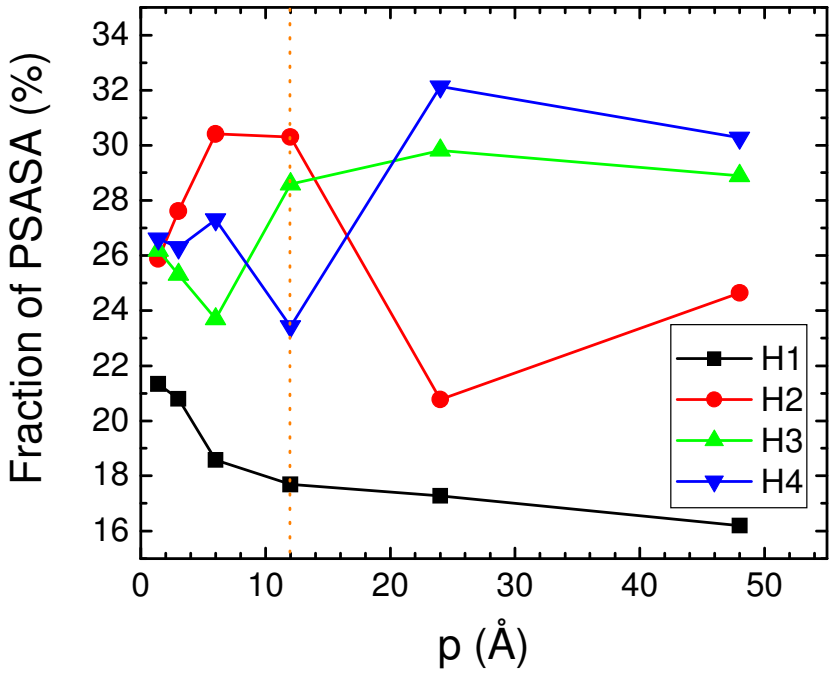

Figure S9. Fraction (in percentage) of partial solvent accessible surface area (PSASA) of the protons of CH_2 groups of G4-NH_2 PAMAM dendrimer calculated using various probe radii. The hydrogen atom type goes outward topologically in the order of H1, H2, H3, and H4. The vertical dotted line highlights the PSASA when p= 12 Å.